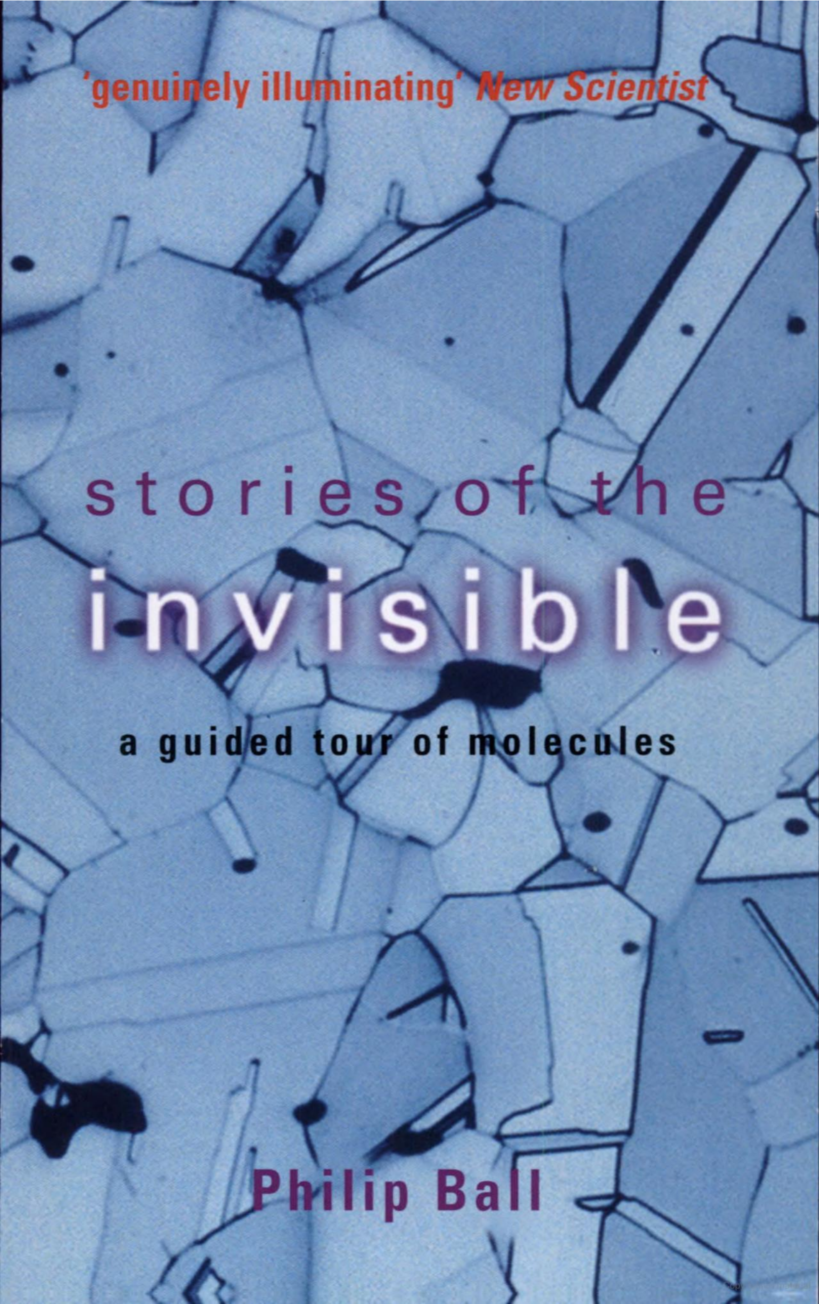

'genuinely illuminating' *New Scientist*

stories of the invisible

a guided tour of molecules

Philip Ball

Stories of the Invisible

A GUIDED TOUR OF MOLECULES

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Engineers of the Invisible

Making Molecules

The sergeant beckoned the waitress, ordered a barley wine for himself and a small bottle of 'that' for his friend. Then he leaned forward confidentially.

—Did you ever discover or hear tell of mollycules? he asked.
—I did of course.
—Would it surprise or collapse you to know that the Mollycule Theory is at work in the Parish of Dalkey?
—Well . . . yes and no.
—It is doing terrible destruction, he continued, the half of the people is suffering from it, it is worse than the smallpox.
—Could it not be taken in hand by the Dispensary Doctor or the National Teachers, or do you think it is a matter for the head of the family?
—The lock, stock and barrel of it all, he replied almost fiercely, is the County Council.
—It seems a complicated thing all right.

The shortest of short introductions to molecules has already been written, and is far more witty than mine. Flann O'Brien was a man who liked to serve up his erudition over a pint of Guinness, as though he were discussing the potato crop or the terrible state of the roads out of Dublin. We can benefit from some more of the wisdom that Sergeant Fottrell is sharing with Mick in the Metropole Hotel, on Dublin's main street:

> —Did you ever study the Mollycule Theory when you were a lad? he asked. Mick said no, not in any detail.
> —That is a very serious defalcation and an abstruse exacerbation, he said severely, but I'll tell you the size of it. Everything is composed of small mollycules of itself, and they are flying around in concentric circles and arcs and segments and innumerable various other routes too numerous to mention collectively, never standing still or resting but spinning away and darting hither and thither and back again, all the time on the go. Do you follow me intelligently? Mollycules?
> —I think I do.
> —They are as lively as twenty punky leprechauns doing a jig on the top of a flat tombstone. Now take a sheep. What is a sheep but only millions of little bits of sheepness whirling around doing intricate convulsions inside the baste.

What is a sheep? This simple question is (under many guises) more than enough to have kept scientists occupied for hundreds of years, and will continue to do so for many years to come. The science of molecules gives an answer embedded in a hierarchy of answers. It is concerned with the 'millions of little bits of sheepness', which are called molecules. A sheep is a blend of many kinds of molecule—tens of thousands of different varieties. Many of them appear not only in sheep but in humans, in the grass, in the skies and oceans.

But science, seeking deeper levels of understanding, does not leave things there. Are not a sheep's molecules made of atoms, and are not atoms made of subatomic particles such as electrons and protons, and are not those made of sub-subatomic particles such as quarks and gluons, and who is to say what *they* contain within their absurdly tiny boundaries?

> —Mollycules is a very intricate theorem and can be worked out with algebra but you would want to take it by degrees with rulers and cosines and familiar other instruments and then at the wind-up not believe what you had proved at all. If that happened you would have to go back over it till you got a place where you could believe your own facts and figures as exactly delineated from Hall and Knight's Algebra and then go on again from that particular place till you had the whole pancake properly believed and not have bits of it half-believed or a doubt in your head hurting you like when you lose the stud of your shirt in the middle of the bed.
>
> —Very true, Mick decided to say.

It is indeed an intricate business to work out what molecules are, if you want to begin on a lower (we should perhaps say deeper) rung of the ladder of science and climb upwards. That is necessary if one wishes fully to understand why molecules behave the way they do, and in consequence why matter—why a sheep or a rock or a pane of window glass—displays its characteristic gamut of properties. But many scientists who work with molecules do not need to bother with all the algebra, for its implications can be generally boiled down to rules of thumb about how molecules interact with one another. The chemical industry was a thriving enterprise before chemistry found its mathematics. Which is a way of saying that molecules need not, after all, make your head hurt.

Leaving the table

It is curious that, when Flann O'Brien reworked the conversation between Sergeant Fottrell and Mick from *The Dalkey Archive* into his most famous novel *The Third Policeman*, published after his death in 1966, he systematically replaced the 'Mollycule Theory' with the 'Atomic Theory'. Here then is the very item, the ambiguity about what things are made from. Is it atoms or molecules? Chemists give out mixed messages. Their iconic cryptogram is the Periodic Table, a list of the ninety-two natural elements (supplemented by some unstable, artificial ones) arranged in a pattern that helps chemists make sense of them. The most famous book 'about' chemistry is the one that Italian chemist and writer Primo Levi named after this tabulation of matter's building blocks, and it reinforces the impression that chemistry begins with this irregularly shaped grid of symbols. At school I was encouraged to learn mnemonics encoding the elements in the first two rows of the table, which are the most important. For undergraduate chemistry it was required that one could recite the whole thing from memory, to know that iridium lies at the foot of cobalt, that europium is sandwiched between samarium and gadolinium. Yet I doubt that I shall

Elements: Primo Levi's *The Periodic Table*

There are the so-called inert gases in the air we breathe. They bear curious Greek names of erudite derivation which mean 'the New', 'the Hidden', 'the Inactive', and 'the Alien'. They are indeed so inert, so satisfied with their condition, that they do not interfere in any chemical reaction, do not combine with any other element, and for precisely this reason have gone undetected for centuries. As late as 1962 a diligent chemist after long and ingenious efforts succeeded in forcing the Alien (xenon) to combine fleetingly with extremely avid and lively fluorine, and the feat seemed so extraordinary that he was given a Nobel prize . . .

Sodium is a degenerated metal: it is indeed a metal only in the chemical significance of the word, certainly not in that of everyday language. It is neither rigid nor elastic; rather it is soft like wax; it is not shiny or, better, it is shiny only if preserved with maniacal care, since otherwise it reacts in a few instants with air, covering itself with an ugly rough rind: with even greater rapidity it reacts with water, in which it floats (a metal that floats!), dancing frenetically and developing hydrogen . . .

I weighed a gram of sugar in the platinum crucible (the apple of our eyes) to incinerate it on the flame: there rose in the lab's polluted air the domestic and childish smell of burnt sugar, but immediately afterward the flame turned livid and there was a much different smell, metallic, garlicky, inorganic, indeed contra-organic: a chemist without a nose is in for trouble. At this point it is hard to make a mistake: filter the solution, acidify it, take the Kipp, let hydrogen sulphide bubble through. And here is the yellow precipitate of sulphide, it is arsenious anhydride—in short, arsenic, the Maculinum, the arsenic of Mithridates and Madame Bovary.

Primo Levi, *The Periodic Table* (1975)

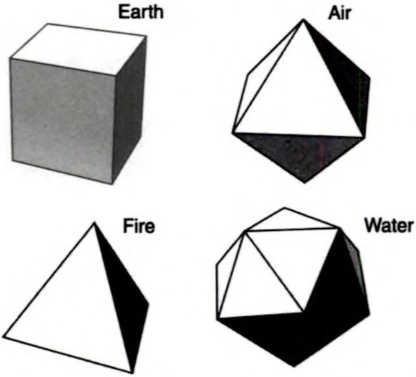
ever set eyes on samarium (although europium shines out at us redly from our television screens).

But chemistry is only incidentally about the properties of the elements, and the science of molecules can afford to ignore many if not most of them. The Periodic Table really belongs to that realm where chemistry becomes physics, where we must wheel out the algebra and the cosines to explain why atoms of the elements form the particular unions called molecules. The table is one of the most beautiful and profound discoveries of the nineteenth century, but, until quantum mechanics was invented by physicists in the twentieth century, one could look upon it only as a mysterious cipher, a kind of crib sheet that served as an empirical reminder that elements come in families whose members show similar proclivities.

Perhaps I am being too quick to dispense with the Periodic Table. At least, I should not do so without confessing to an agenda.

A conventional history of chemistry presents it as a quest to understand matter: to ask, what are things made of? This links chemistry with ancient Greek philosophy, with the attempts of Leucippus and his pupil Democritus to formulate an atomic theory of matter in the fifth and fourth centuries BC. It gives us a narrative that progresses from Empedocles' four elements—earth, air, fire, and water—through to Plato's marriage of elemental theory with atomism (Fig. 1), skirting cautiously around the medieval alchemists' belief in the transmutation of the elements and alighting gingerly on the phlogiston theory of the eighteenth century. We watch

Robert Boyle redefine the idea of an element in 1661 (which, however, does not actually amount to much of a redefinition at all), we see antiquity's four-element scheme crumble before the discovery of new 'irreducible substances', and we see Antoine Lavoisier dismantle phlogiston and replace it with oxygen before losing his head under the guillotine's blade in 1794. John Dalton gives us the modern atomic theory in 1800, the list of elements expands enormously throughout that century, and then Dmitri Mendeleev arranges them into the twin-towered edifice of the Periodic Table. The gaps are gradually filled all the way up to uranium (itself known since 1789), and Wolfgang Pauli and the other



1 Plato's atoms. The Greek philosopher believed that the smallest particles of the four elements then thought to comprise everything had regular geometric shapes

quantum physicists explain the table's shape in the 1920s.

And so the task is at an end. According to science writer John Horgan in *The End of Science*, this meant that chemistry too was finished, once it had the quantum stamp of approval. The implication in several other recent books on the future of science is that the discipline, conspicuous by its absence, has been consumed from both ends. At the most fundamental level, it has become physics (including that immense but overlooked branch called condensed-matter physics, which ponders on how tangible matter behaves). At the most complex level, it is now the domain of biologists, who have expanded their world to embrace the molecular mechanics of the cell.

But these academic turf wars conceal a far more interesting truth. It is a curious fact that many histories of science are written by physicists, who have a tendency to present science as a series of questions posed and then answered. It would be instructive to see the story told instead by an engineer, whose instinct might rather be to ask: what can we make? For, while some of our proto-chemists were wishing to dissect matter, whether physically or metaphysically, others were eagerly rearranging it. This is why the science of molecules is both a creative as well as an analytical pursuit. It has been, at various times in history, concerned with making ceramic pots, dyes and pigments, plastics and other synthetic materials, drugs, protective coatings, electronic components, machines the size of a bacterium. 'What is strange', says chemistry Nobel laureate Roald Hoffmann, 'is that chemists should accept the metaphor of discovery'. He goes on:

> Chemistry is the science of molecules and their transformations. Some of the molecules are indeed *there*, just waiting to be known by us . . . But so many more molecules of chemistry are made by us, in the laboratory . . . At the heart of [chemistry] is the molecule that is made, either by a natural process or by a human being.

Universities that hide their chemistry departments under the banner of 'molecular sciences' are possibly onto the right idea; for this gently releases the ballast of the Periodic Table and leaves the chemist free to ascend into a world of synthesis, a non-Platonic realm where molecules are designed and made to *do* things, such as cure viral infections or store information or hold bridges together.

As an industrial chemist, Primo Levi moved in this world. He felt a little apologetic about his molecular science: he called it 'a "low" chemistry, almost culinary'. But the power of 'low' chemistry is awesome. It shifts billions of dollars each year, it can make the sick healthy and the healthy sick. Hamburg and Dresden were laid waste by low chemistry, and chemical and biochemical warfare are now more feared in the West than nuclear war. Many people believe that the nuclear bomb was itself the product of physics, but writing $E = mc^2$ does not give you Hiroshima—only separating isotopically distinct molecules of uranium compounds did that. In *Gravity's Rainbow*, Thomas Pynchon has no doubt where the true power of science lies: the villain of his fantasy from the fag-end of the Second World War is not the Bomb but a new plastic, an 'aromatic heterocyclic polymer' called Imipolex G, developed in a conspiracy between Europe's giant chemicals companies IG Farben, Ciba, Geigy, Shell Oil, and ICI. The message is that 'stuff' speaks louder than theories.*

Does this mean that molecular science is bad? Of course not—it means that it is a craft full of possibilities. Wonderful, inspiring, inventive possibilities. Terrible, nightmarish possibilities. Mundane but useful things, bizarre things, hard-to-understand things. Molecular science might one day help people to grow a new liver. Raphael, Rubens, and Renoir painted with molecules. Molecules orchestrated the origin of life.

What are molecules?

So molecules make up everything there is? Not exactly. All matter (outside of some strange astrophysical environments) is made up of atoms; but atoms do not always organize themselves into molecules. (I cannot tell whether Flann O'Brien made the switch from 'mollycules' to atoms because he understood, or did not understand, this distinction.) Most atoms on their own are highly reactive—they have a

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* After the end of the war, a group from the Allies assembled by Eisenhower claimed that 'Without IG [Farben]'s immense productive facilities, its far-reaching research, varied technical experience and overall concentration of economic power, Germany would not have been in the position to start its aggressive war in September 1939.' It was one of IG Farben's subsidiary companies, Degesch, that made the poison gas Zyklon B used in the concentration camps.

Synthesis: Thomas Pynchon's *Gravity's Rainbow*

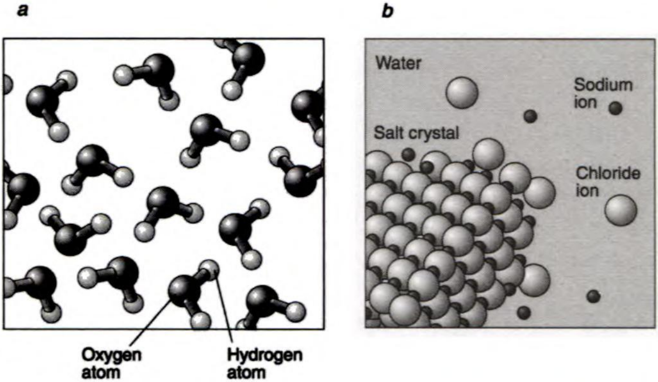
The origins of Imipolex G are traceable back to early research done at du Pont. Plasticity has its grand traditions and main stream, which happens to flow by way of du Pont and their famous employee Carothers, known as the Great Synthesist. His classic study of large molecules spanned the decade of the twenties and brought us directly to nylon, which is not only a delight to the fetishist and a convenience to the armed insurgent, but was also, at the time and well within the System, an announcement of Plasticity's central canon: that chemists were no longer to be at the mercy of Nature. They could decide now what properties they wanted a molecule to have, and then go ahead and build it . . . A desired monomer of high molecular weight could be synthesized to order, bent into its heterocyclic ring, clasped, and strung in a chain along with the more 'natural' benzene or aromatic rings. Such chains would be known as 'aromatic heterocyclic polymers'. One hypothetical chain that Jamf came up with, just before the war, was later modified into Imipolex G.

Thomas Pynchon, *Gravity's Rainbow* (1973)

predisposition to join up with other atoms. Molecules are collectives of atoms, firmly welded together into assemblies that may contain anything up to many millions of them.

But there is a further, subtle distinction to be made. Flann O'Brien's Sergeant Fottrell speaks of 'mollycules' of rock and of iron. Strictly speaking, there are no such things—at least, not in a block of everyday rock or iron. By molecules, we generally mean assemblies of a discrete, countable number of atoms. In the water molecule there are three atoms: two of hydrogen and one of oxygen. A glass of water contains trillions upon trillions of atoms, but a snapshot of the liquid—were it able to reveal such tiny details—would show that at any instant they are nearly all grouped into these three-atom molecules, like a gigantic crowd holding hands in families of three (Fig. 2*a*).

The atoms in iron, in contrast, do not cluster into discrete molecules. They stack together like cannonballs in a regular array that goes on and on, like a regimented battalion of



2 Water (*a*) is composed of discrete three-atom molecules, joined by strong chemical bonds. Salt (*b*), in contrast, is an assembly of charged atoms (ions) of sodium and chlorine, in which there are no discrete atomic groupings. When salt dissolves in water, the assembly merely falls apart ion by ion

soldiers. One cannot identify any grouping of the atoms—each is equidistant from its neighbours. The same is true of sodium and chlorine atoms in a crystal of sodium chloride (table salt (Fig. 2*b*)). When iron melts, the atoms simply jostle one another like an unruly crowd. But when ice melts, it is as if the hydrogen and oxygen atoms continue to hold hands in threes as the crystal falls apart. One would say that ice is a molecular solid—the atoms are clustered into molecules—whereas iron and rock salt are not.

Some pure elements adopt molecular forms; others do not. As a rough rule of thumb, metals are non-molecular, like iron, whereas non-metals are molecular. Frozen nitrogen, for instance, consists of molecules containing two atoms each. In phosphorus the atoms form groups of four; in sulphur they can link into molecular rings of eight. It seems a little unfair that there is no way of knowing, simply by looking at a material, if its essential building blocks are atoms or molecular unions of atoms. But there is not. (It is not hard for scientists to find out, however.)

So 'molecule' is actually a rather fluid, loosely defined concept—essentially a question of scale. Why bother, then, to single out molecules at all, rather than simply talking about 'matter' in general? I would suggest the following reason: molecules are the smallest units of *meaning* in chemistry. It is through molecules, not atoms, that one can tell stories in the sub-microscopic world. They are the words; atoms are just the letters. Of course, sometimes a single letter constitutes a word. But most words are distinct aggregates of several letters arranged in a particular order. We often find that longer words convey subtler and more finely nuanced meanings. And in molecules, as in words, the order in which the component parts are put together matters: 'save' and 'vase' do not mean the same thing.

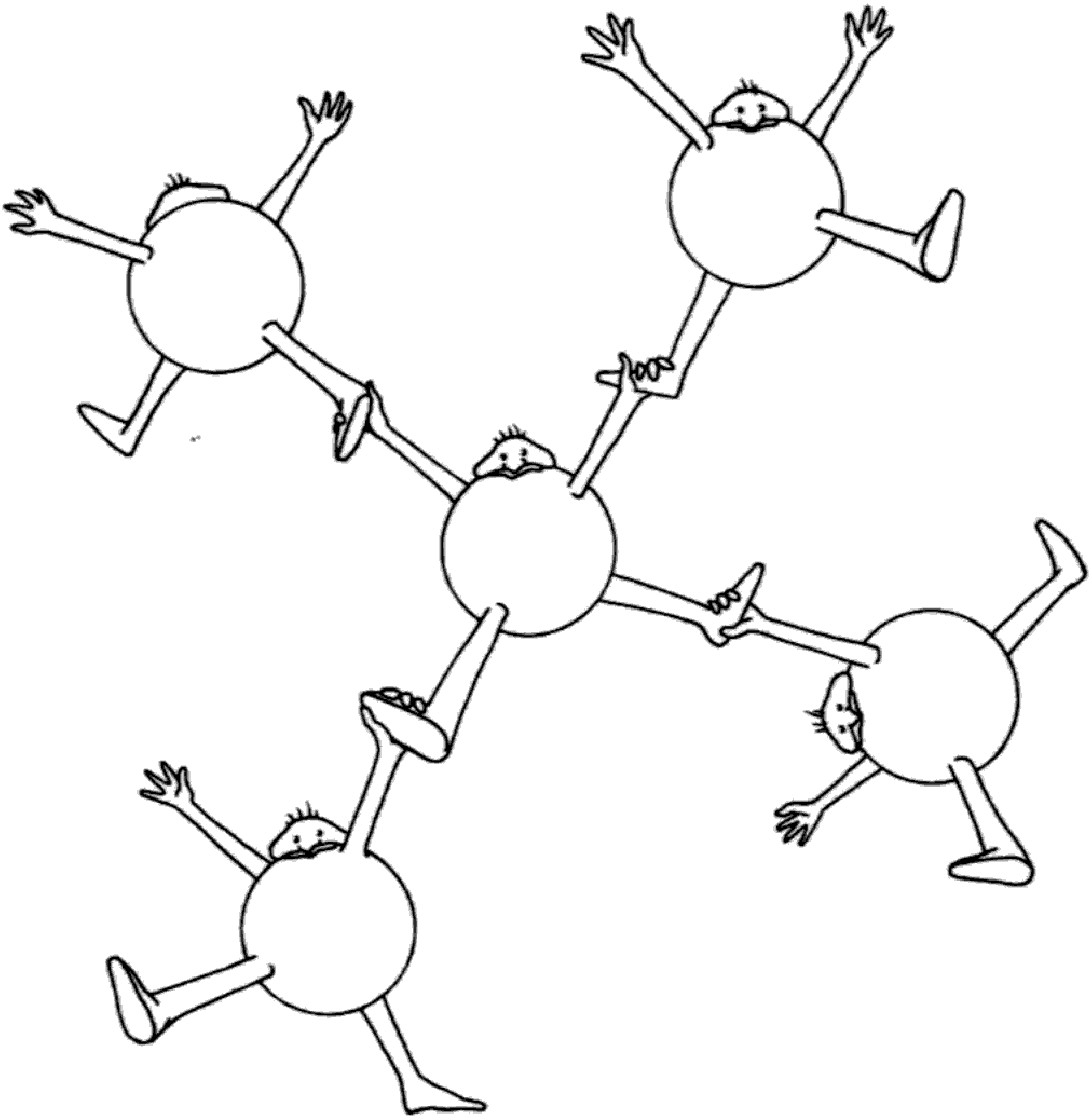
Some of the most wondrous stories told by molecules take place in living organisms. But unfortunately they can be very difficult to understand: many of the words are long and unfamiliar, and we have only a dim grasp of the syntax. Chemists are constantly inventing new molecular words, expanding the language—and some of these neologisms are rather witty. Some let us tell tales that could not even be formulated before the 'word' was invented. In other cases, a new 'word' allows us to say in a simple manner something that was previously conveyed in a roundabout way.

It is remarkable how nicely the linguistic metaphor fits the molecular world. We hear much today about the 'language of the genes', and I hope to show that this is just one of the tongues that molecules encode. Yet it is not merely a metaphor. There really is 'information' in molecules, just as there is in words, as I show in Chapter 7.

Moreover, using an information-based paradigm to describe molecular science is valuable in so far as it invites a responsive, dialogue-based description rather than the mechanical one that has been championed in former times. Cell biologists speak increasingly about protein molecules that 'talk to' one another; physicists interested in the science of matter speak of 'cooperative' and 'collective' behaviour. These are not woolly, romantic notions calculated to make science appear friendlier (although it will do no harm if they have that effect). Rather, they speak of the increasing awareness of the beautiful sophistication of molecular behaviour, which is generally gregarious and rarely linear.

It is with these thoughts in mind that I need to expand on the use of metaphor in molecular science. We cannot do without it, even at the level of one specialist speaking to another. This is true in many areas of science, but in chemistry more than most. Molecules are anthropomorphized mercilessly, and there need be no apology for that. They are unfamiliar things, these molecules, and we need to find ways of making them less so. The publishers of my book about water rightly insisted that ball-and-stick models of H_2O molecules were anathema to the non-chemist reader, guaranteed to ensure that the book stays on the shelf. Yet I could not explain water's strangeness without showing its molecular structure, and so I made the molecules into little demons (Fig. 3).

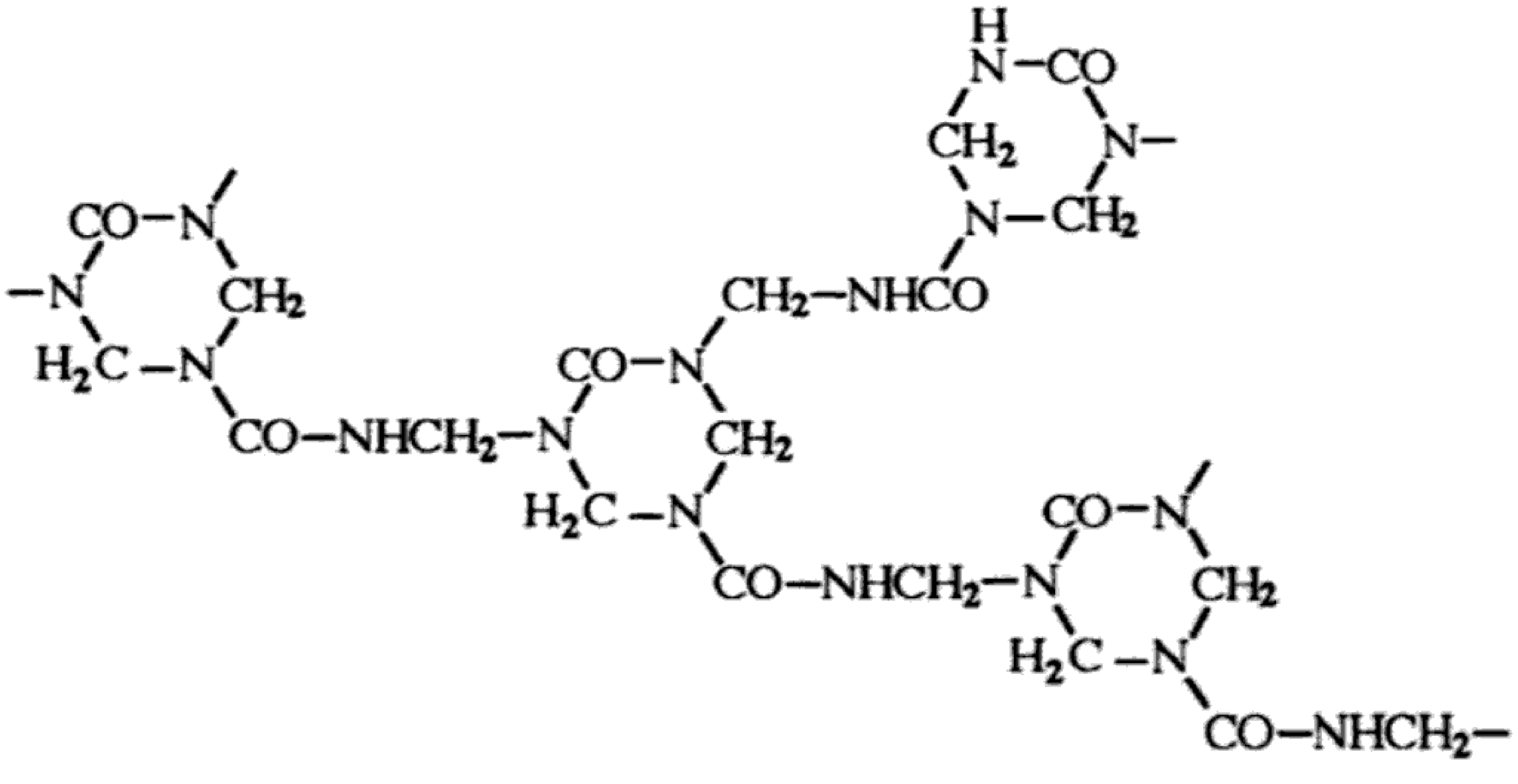
I hope this was harmless. But I was reminded of the dangers at a public lecture I attended recently on molecular replication. The first question from the floor was 'Are these molecules conscious?' Given that the speaker was talking about a synthetic molecular system that mimics (in a very crude way) some of the characteristics of living organisms, I suppose this was an understandable enquiry. I firmly believe the answer is 'no', if one wants to retain any meaningful working definition of the slippery concept of consciousness. But, once we start to anthropomorphize, we import a baggage of associations, for better or worse. Many people hate the concept of 'selfish genes' because it carries moral



3 Making molecules anthropomorphic can help us visualize how they interact. Here I show the weak 'handclasps' that exist between water molecules connotations. (Richard Dawkins calls it 'poetic science', and I can see what he means—but the poetry of the mechanism gets besmirched by the unpleasantness, as many see it, of the metaphor.) The idea that molecules 'cooperate' and 'communicate' is no basis for a philosophy of nature. But it is reason to suspect that, in molecular science at least, a linear, clockwork world view might in the end leave us like the ancient astronomers interpreting planetary motions from a geocentric perspective: trying to shoehorn the observations into a misconceived framework.

Shape and size

Primo Levi's *The Monkey's Wrench* is one of the few novels I can think of that includes a drawing of a molecule (Fig. 4). It



4 Primo Levi's molecule

is a fearsomely complicated one, and I would never dream of showing it in a non-technical book about science if my intention was to be instructive.

But Levi gets away with it, because he does not want us to understand anything about the molecule, except for one thing: it has a shape and structure. There are some kinds of hexagon in here, and some straight units linking them together. The narrator is talking to a construction worker named Faussone, a man who assembles girders into bridges. He says,

> the profession I studied in school and that has kept me alive so far is the profession of a chemist. I don't know if you have a clear idea of it, but it's a bit like yours; only we rig and dismantle very tiny constructions . . . I've always been a rigger-chemist, one of those who make syntheses, who build structures to order, in other words.

We will encounter in these pages examples of molecules that can be regarded as miniature sculptures, containers, soccer balls, threads, rings, levers, and hooks, all made by sticking atoms together. Plato believed that atoms have the shapes of 'regular polyhedra': cubes, tetrahedrons, octahedrons, and so on. He was wrong;* but chemists can arrange atoms into molecules with these shapes.

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* Actually, one can make a case that Plato was not far wrong at all. Atoms do link together in quite precise geometrical arrangements. Carbon atoms, for example, like to sit at the centre of a tetrahedron with four other atoms at the corners. This does not exactly make it the tetrahedral block that Plato envisaged for atoms of 'fire'; but it shows that Plato's geometric view of the microscopic world held a grain of truth.

So how big is this molecule that Levi's narrator draws for Faussone? Each one of those C's, N's, and so forth represents an atom, which is a truly tiny thing. Countless analogies struggle to convey the scale of atoms, but I am not sure that they serve to give an impression any more concrete than that these irreducible particles of the elements are very, very small indeed. For example, if a golf ball were blown up to the size of the Earth, its atoms would be about the size of the original golf gall. Ten million atoms of carbon side by side would make a row about a millimetre long.

A small molecule like water is just a few atoms' width in size, about three-tenths of a nanometre. (A nanometre is a millionth of a millimetre.) Primo Levi's molecule is several times bigger. (One cannot say exactly how many times, because what he drew was really just a fragment of a molecule, which continues to the right and the left of the page.)

One consequence of this scale is that things happen very fast in the molecular world. When we hear that molecules can rotate ten billion times a second, we imagine that they must be spinning at unimaginable speeds. But molecules are so small that, even if they travel at quite moderate speeds, they can cover molecular-scale distances in an instant. The atoms of an oxygen molecule need move only at a speed of about a metre per second to complete ten billion revolutions in a second.

What about the sticks that join the atoms together? In fact, they take up no space; they are just a convention to help us see what is going on in the diagram. Atoms that are bound together in molecules push right up against one another; in fact, they overlap, rather like two soap bubbles in contact. This is possible because atoms are not like hard billiard balls, but more like rubber balls. They have a centre that *is* dense and hard, called the nucleus, and this is about ten thousand times smaller than the atom itself—although it is where nearly all of the atom's mass is concentrated. The nucleus has a positive electrical charge. Surrounding it is a cloud of electrons, which are small, light subatomic particles with a negative charge. The electron clouds of two atoms can overlap without danger of electrons colliding, and the two atoms then share some of their electrons: the two clouds merge into one, encompassing both nuclei. When this happens, the two atoms are said to be linked by a *covalent bond*. The sticks in the molecular diagram on p. 17 represent covalent bonds, and they are just a way of helping us to see which atoms are bonded to which.

Here is one of the crucial considerations in talking about molecules, and it is one that complicates the whole attempt: there is no 'best' way of drawing them. One might say: well, never mind the schematic diagrams, why not show what they 'really' look like? But that does not help, because there is no way of taking a photograph of a molecule in the same way as we can photograph a cat or a tree. This is not a matter of technical limitations—it is not that we lack a microscope or a camera capable of resolving such small objects. The fact is the mechanics of seeing make it impossible to 'see' a molecule (or an atom, for that matter) 'as it really is'.

The reason is that we see with visible light, which is a wave-like radiation for which the wavelength—the distance between successive crests—varies from about 700 nanometres for red light to 400 nanometres for violet light. In other words, red light fits about 140,000 undulations into a centimetre. This wavelength is hundreds of times larger than a molecule. Roughly speaking, light cannot be focused to a point smaller than its wavelength, which means that objects smaller than that cannot be resolved.* No light-based microscope will ever show us a sharp image of a water molecule.

I suspect that this is one reason why people find molecules hard to comprehend, and why diagrams like the one above are a good way to scare readers away from a science book. It seems absurd to be talking in a concrete manner about objects that are not only too tiny to see in practice but too tiny to see in principle. Things that cannot be seen acquire an aura of fantasy, as though they are just a convenient fiction.

Molecules are not a fiction, however, and we can prove not only that they are there but that they have definite shapes and sizes. Fig. 5 shows some portraits of molecules taken with a special kind of microscope that does not use light to form its images. Beside each snapshot I show a diagram of the molecule's structure. Well before this type of microscope was invented, the molecules were known to possess these

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* I'm speaking here of conventional microscopy, where the light is focused by lenses. There are some new optical (light-based) microscopes that surpass this wavelength-limited resolution by getting the light source up close to the sample and shining it through a tiny aperture. This can increase the resolution to, so far, around a tenth of a wavelength.

'The molecular nature of life is not a gallery but a dance.'

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